Neurovascular responses to simulated deep **space radiation** in a human organ-on-a-chip model

Biological and Physical Sciences

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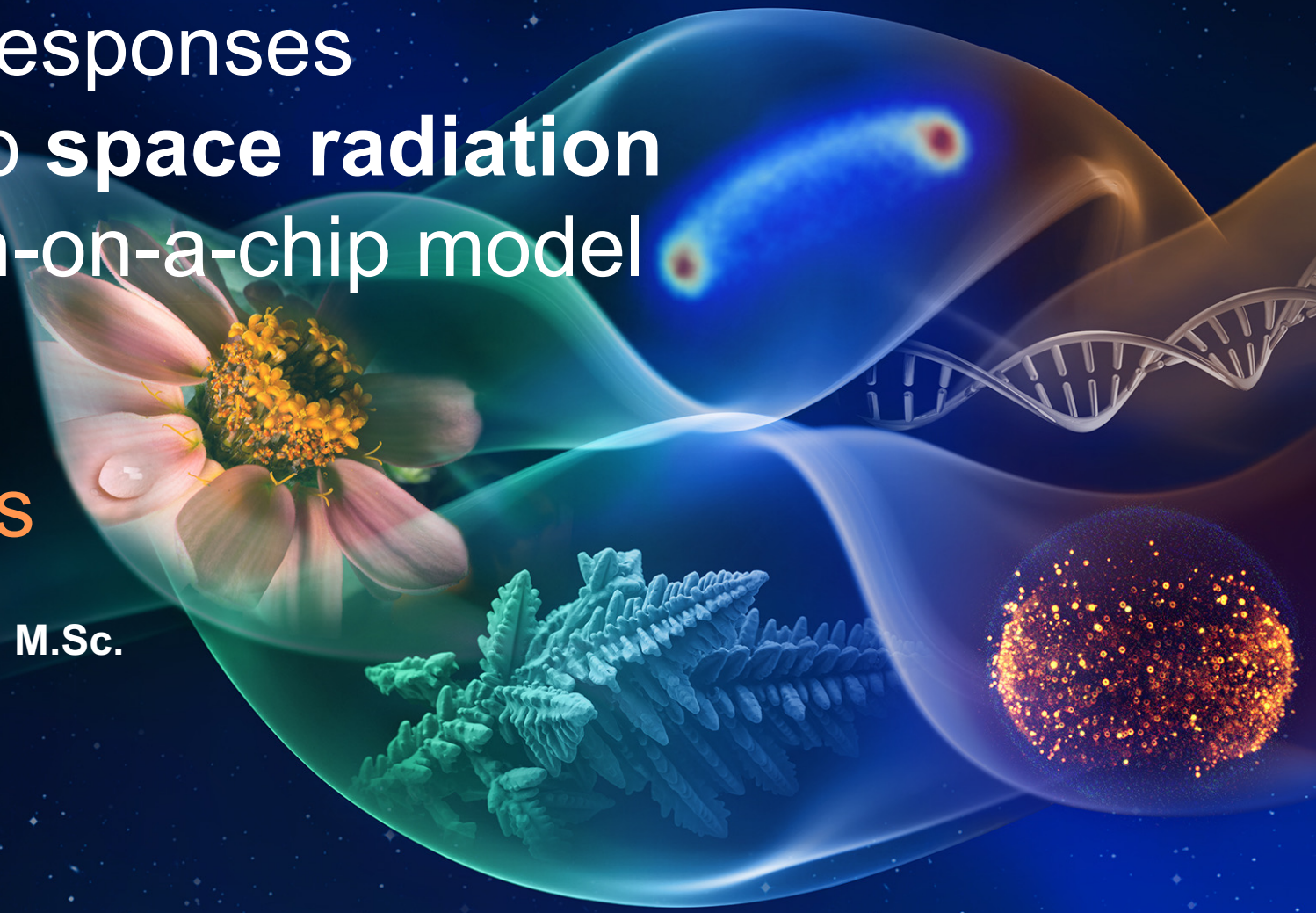

Blue Marble Space
Institute of Science

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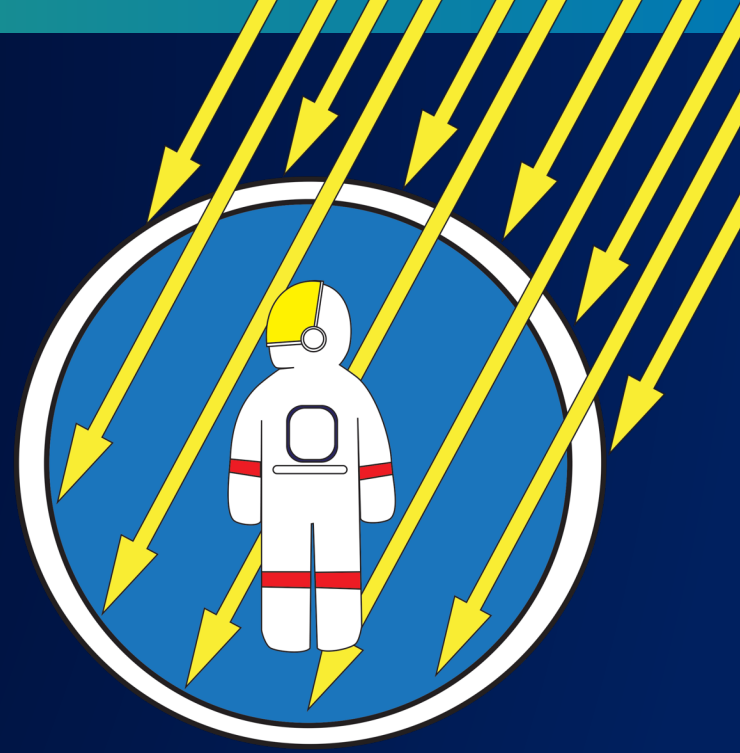
Distance from Earth

5 HAZARDS of Human Spaceflight

Isolation
& Confinement



Radiation

Hostile/Closed
Environments

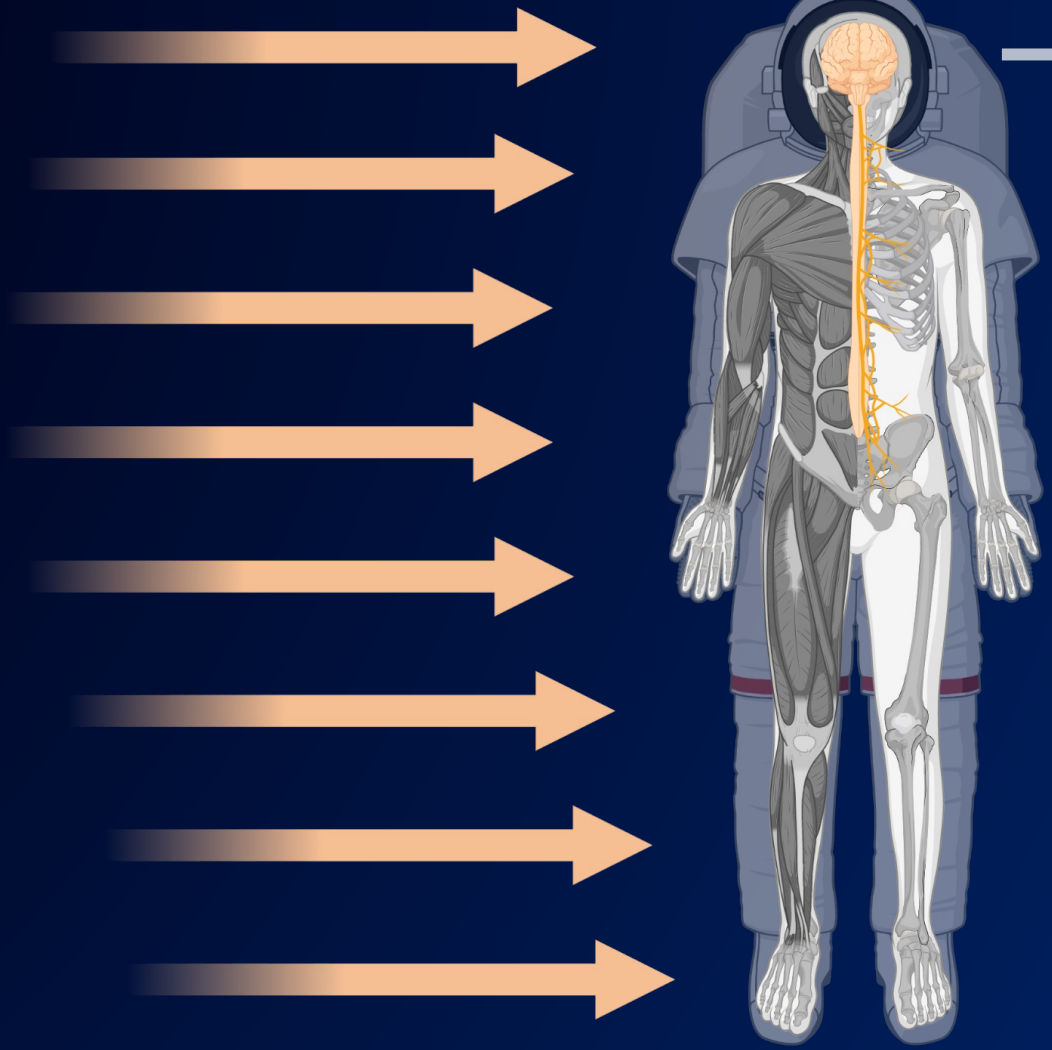
Altered Gravity

www.nasa.gov/hrp

GCR

GALACTIC COSMIC RAYS

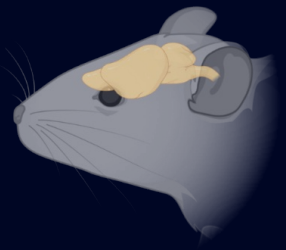
~87% protons
~12% ^{4}He
~1% high mass-energy particles through ^{56}Fe



Central Nervous System Risks

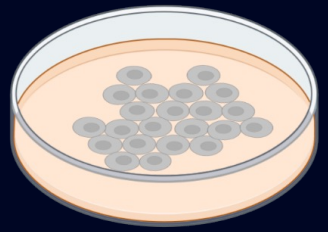
All figures are produced using biorender.com

Your Brain in Space – How to Model?



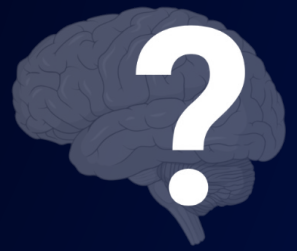
Animal models

+



2D cell culture

+

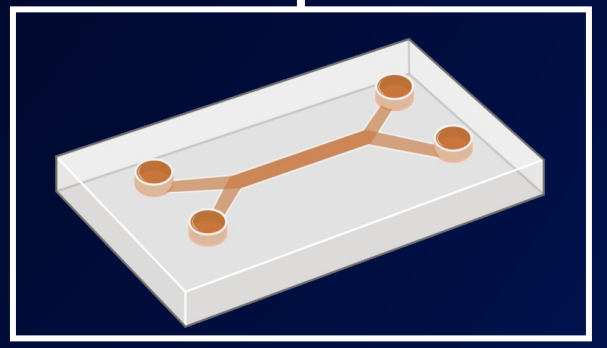


New models?

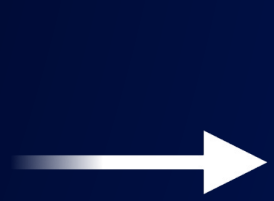
human

3D

multicellular

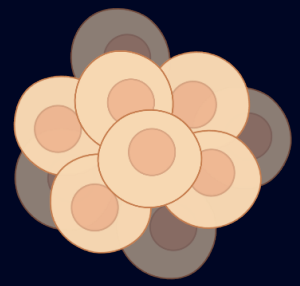


Organs-on-chips

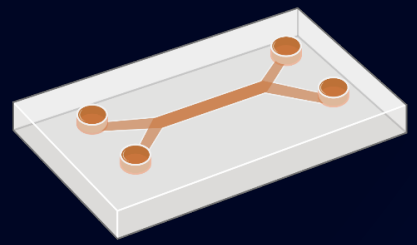


Organ Models for Deep Space Exploration

High throughput, small footprint, automated, multi-organism



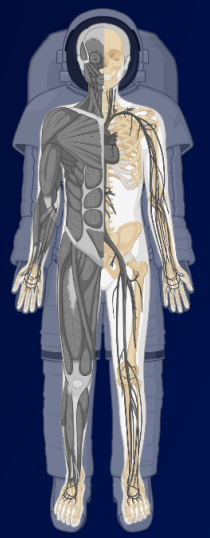
Primary cells



Organs-on-chips

Simulated spaceflight stressors: microgravity, ionizing radiation

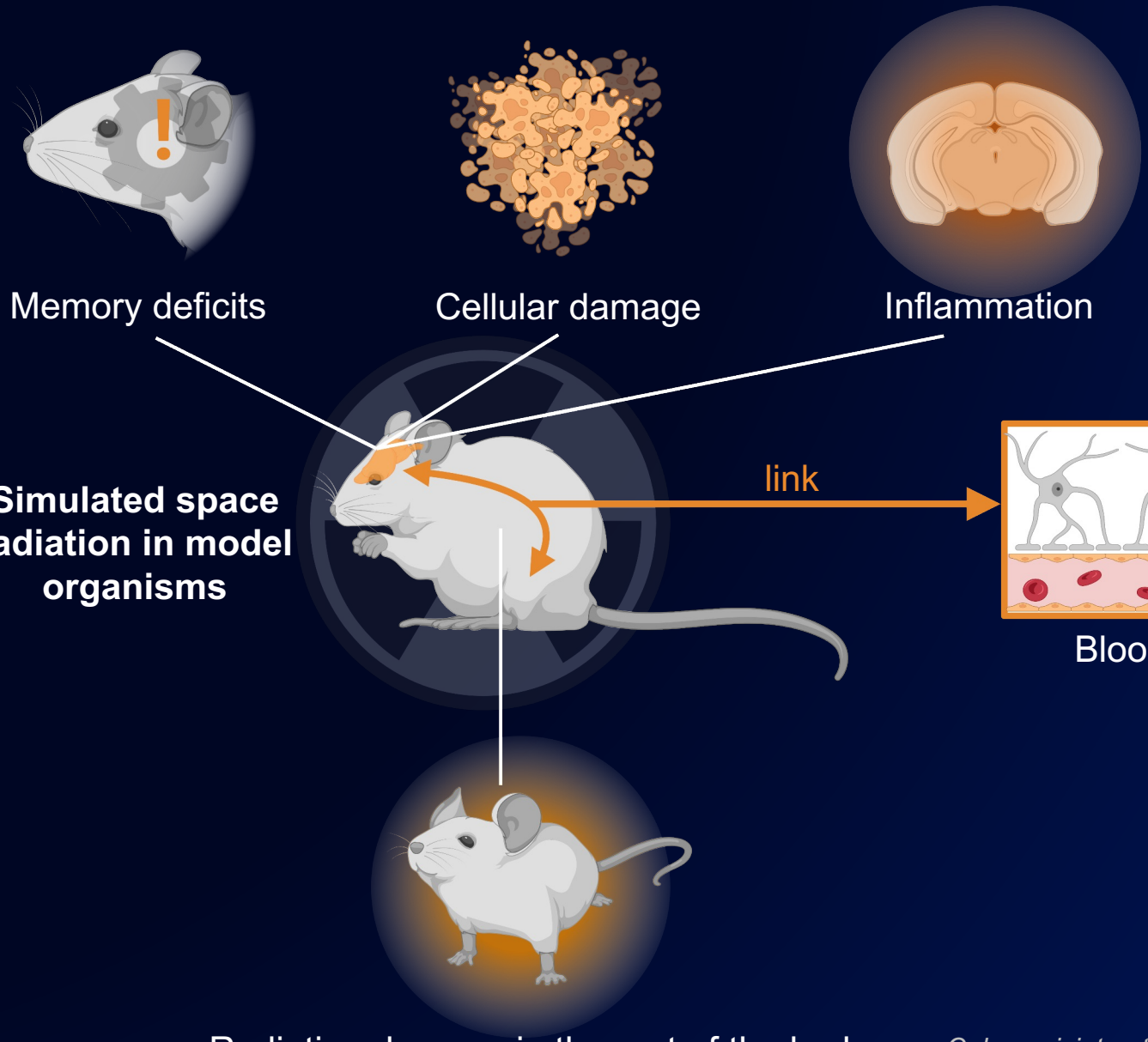
Payloads in and



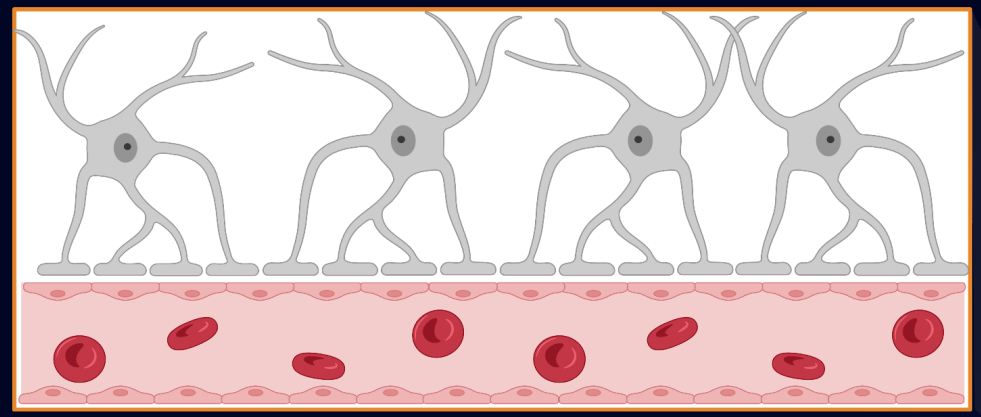
- **Biological responses to spaceflight**
- **Biomarkers**
- **Countermeasures**
- **Comparison with terrestrial diseases**

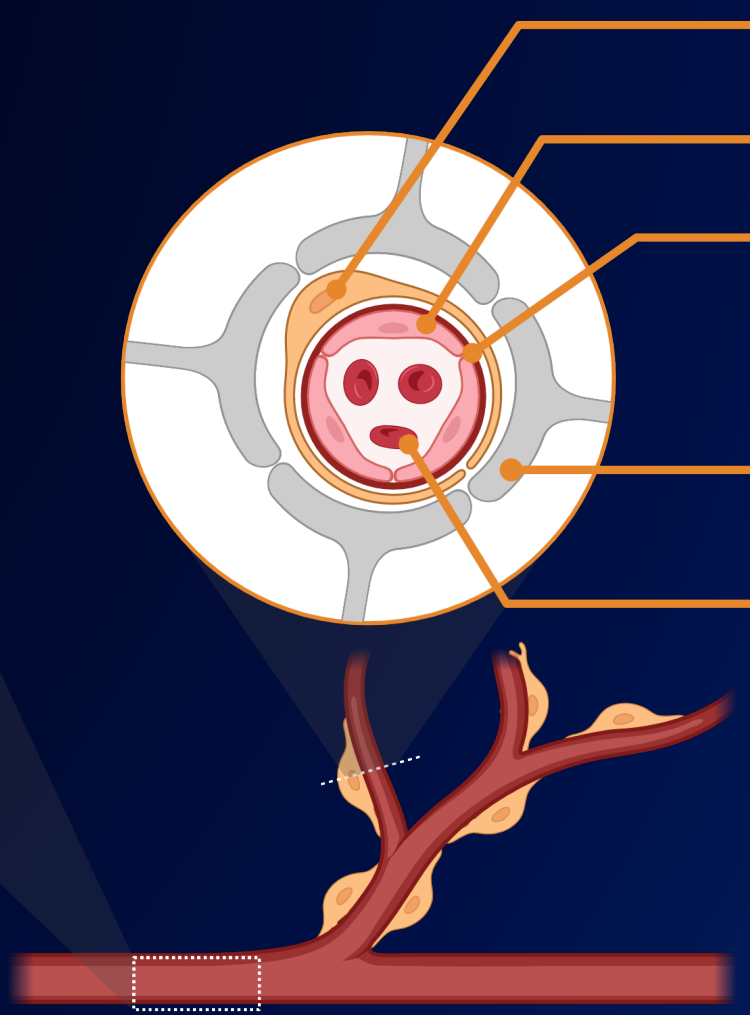
BLOOD BRAIN BARRIER ON A CHIP

Neuroimmune Effects of Space Radiation



The Blood-Brain Barrier





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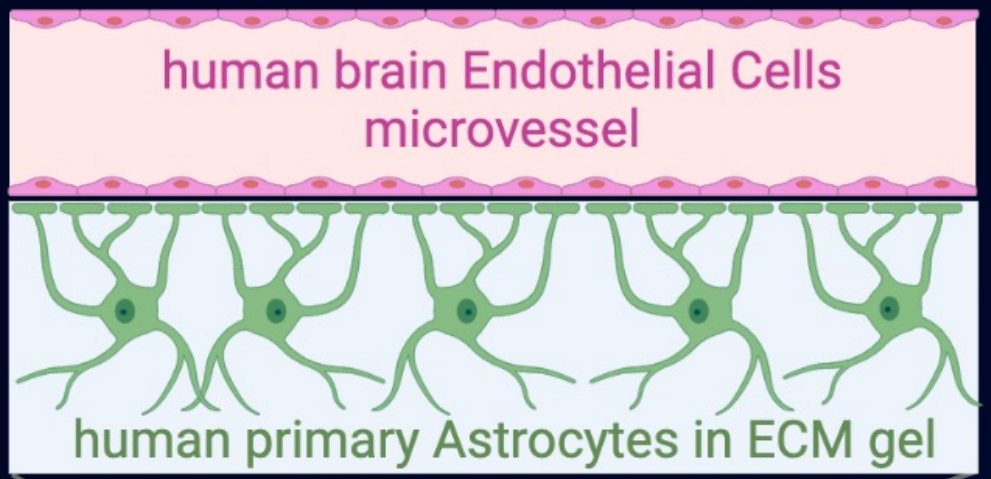
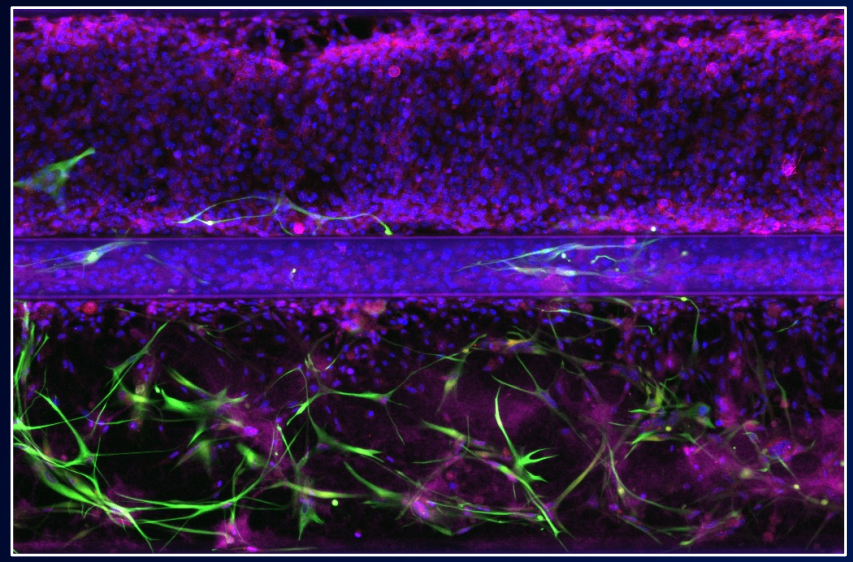
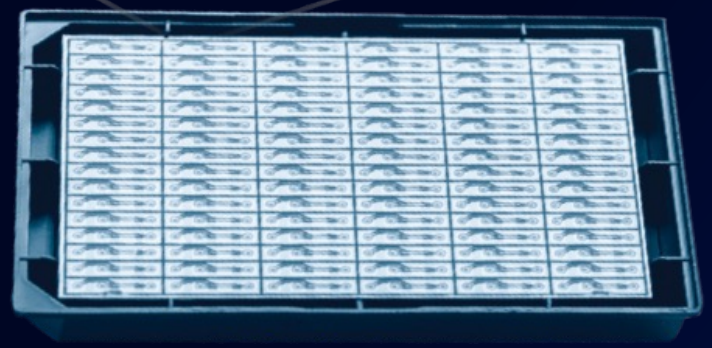
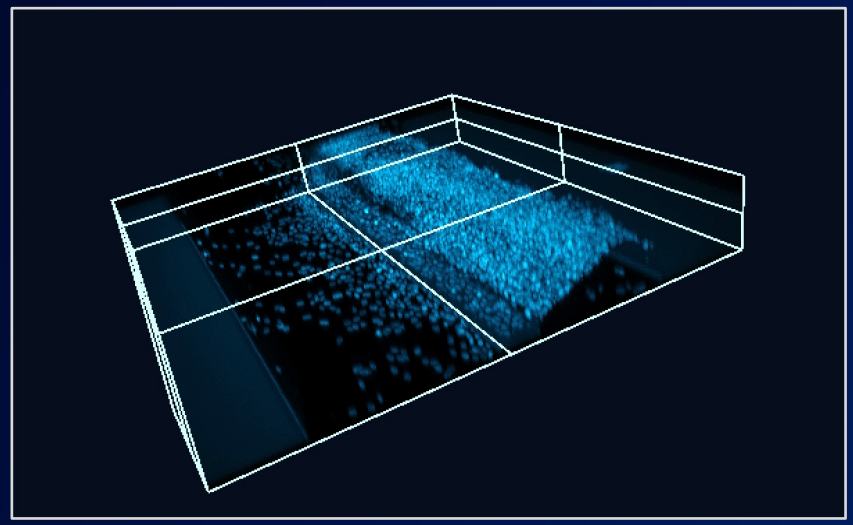
Neurovascular Model





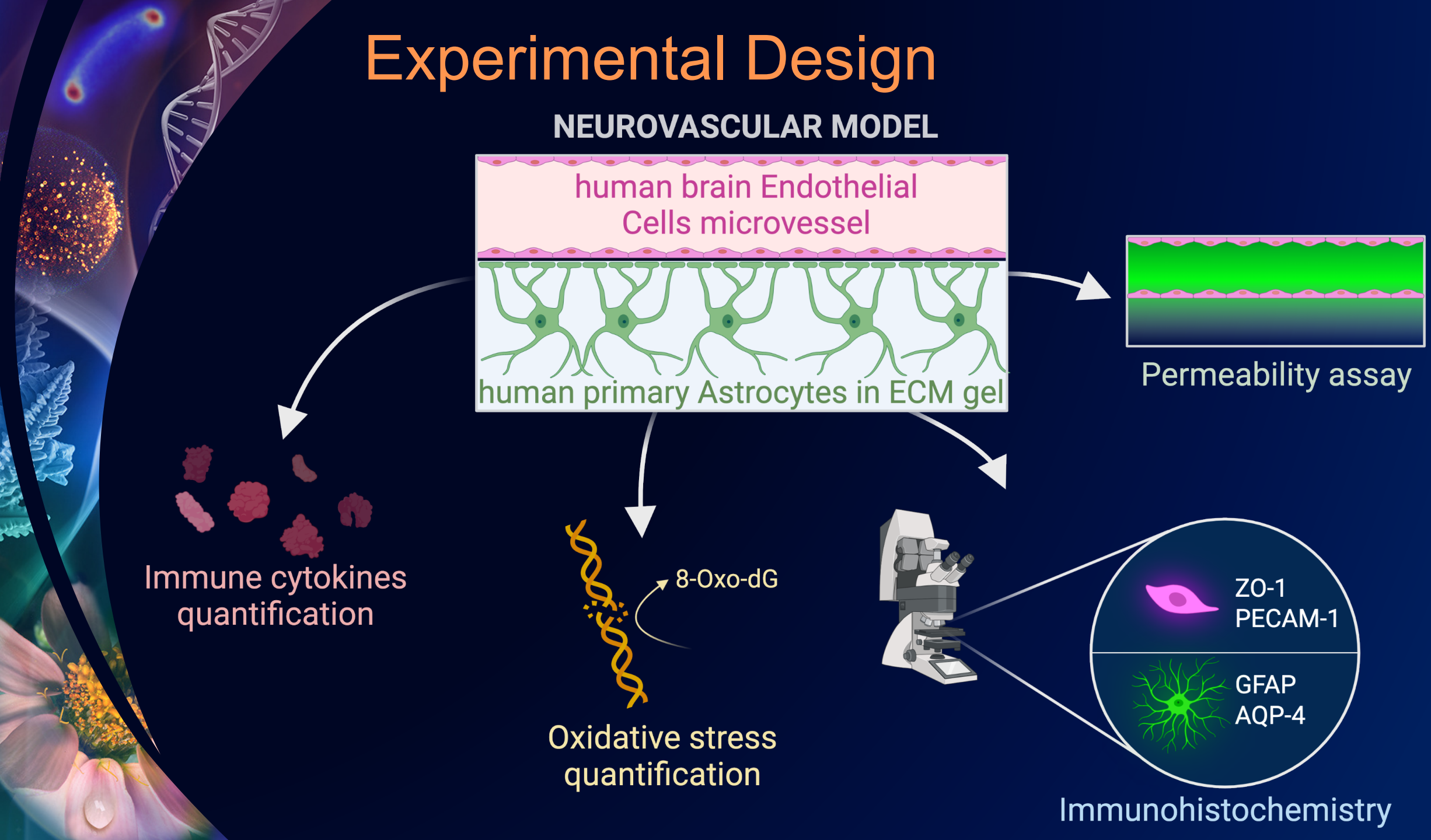


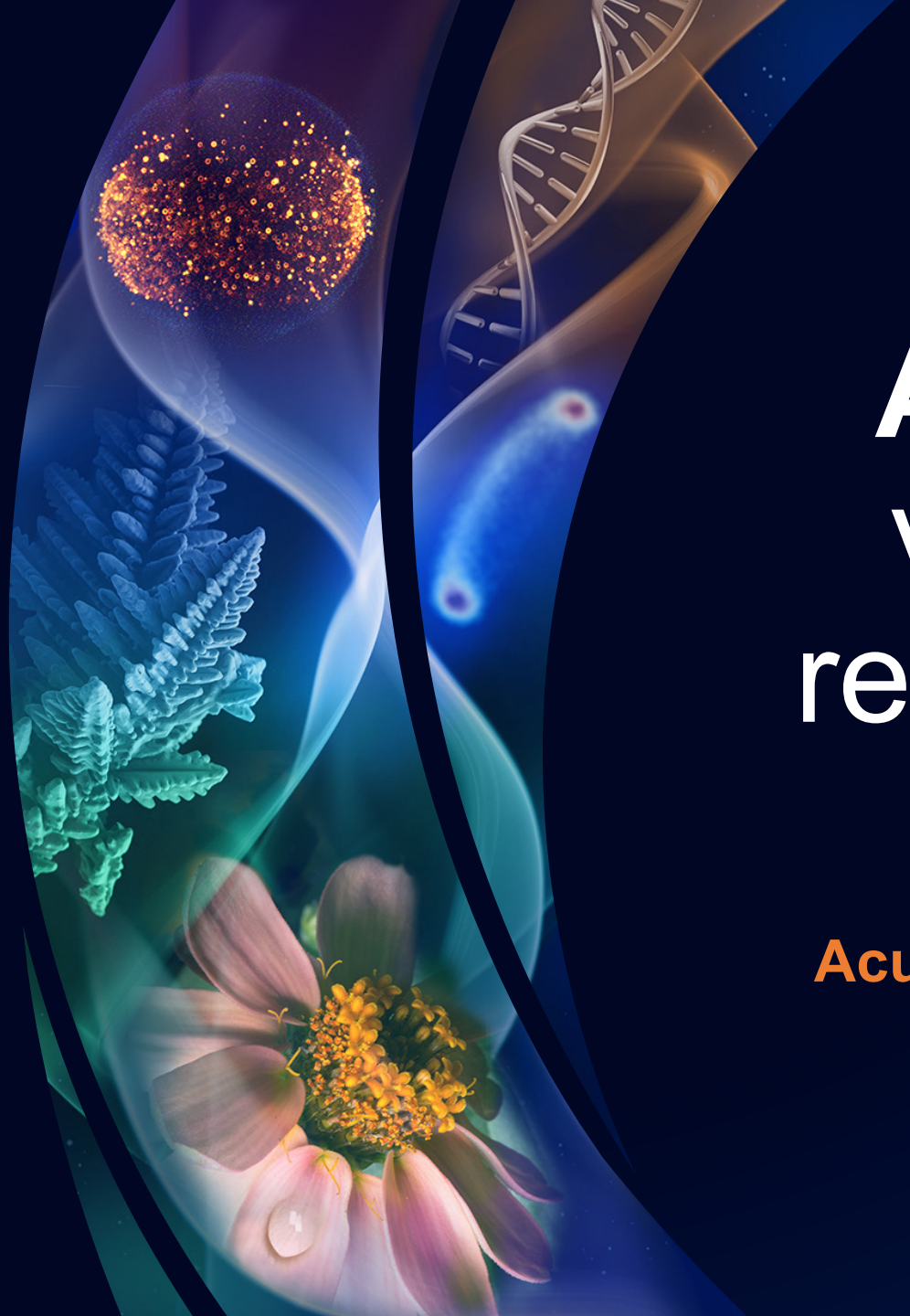
OrganoPlate® 2-lane



Verma *et al*., Astrocytes regulate neurovascular responses to simulated deep space radiation in a human organ-on-a-chip model. *Front Immunol,* 2022, p. 4990

Experimental Design



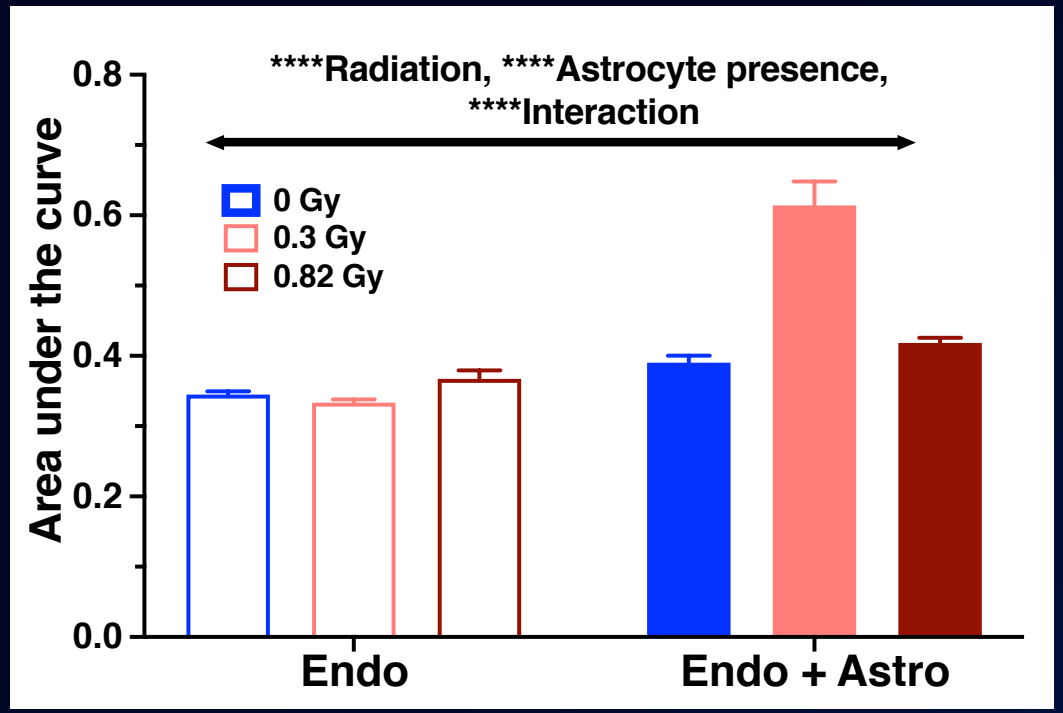


Astrocytes regulate vascular endothelial responses to simulated space radiation

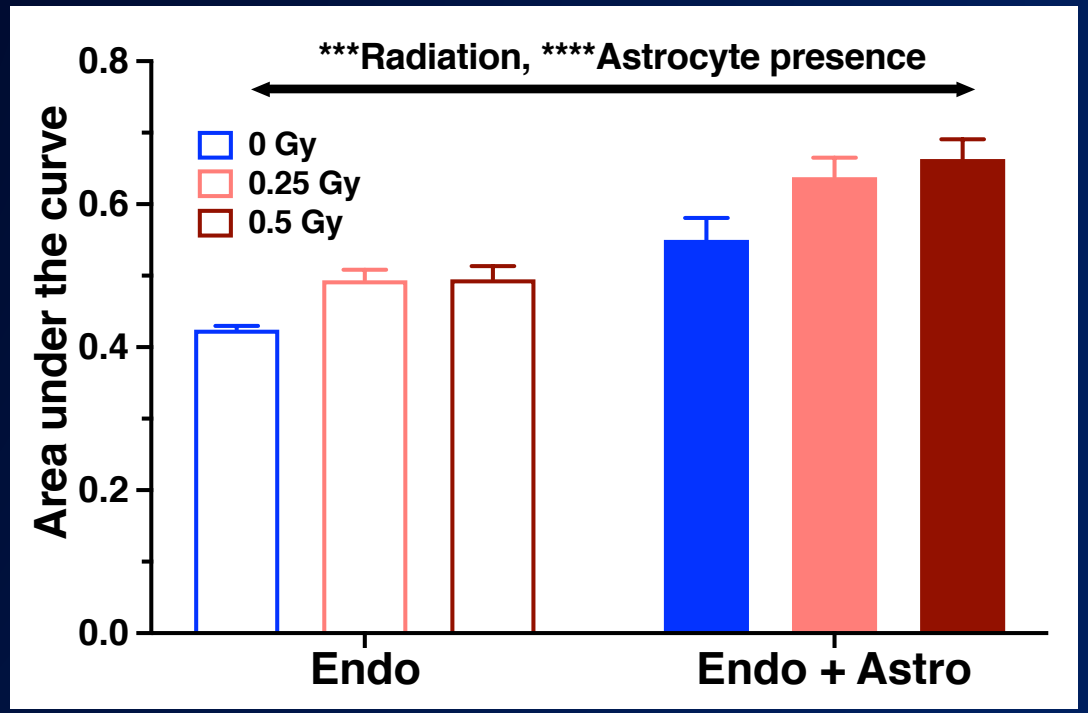
Acute and **subacute** responses to simulated GCR

Acute Responses to Radiation:
Blood-Brain Barrier Permeability Exacerbated by Astrocytes

600MeV/n ^{56}Fe particles



Simulated Galactic Cosmic Rays



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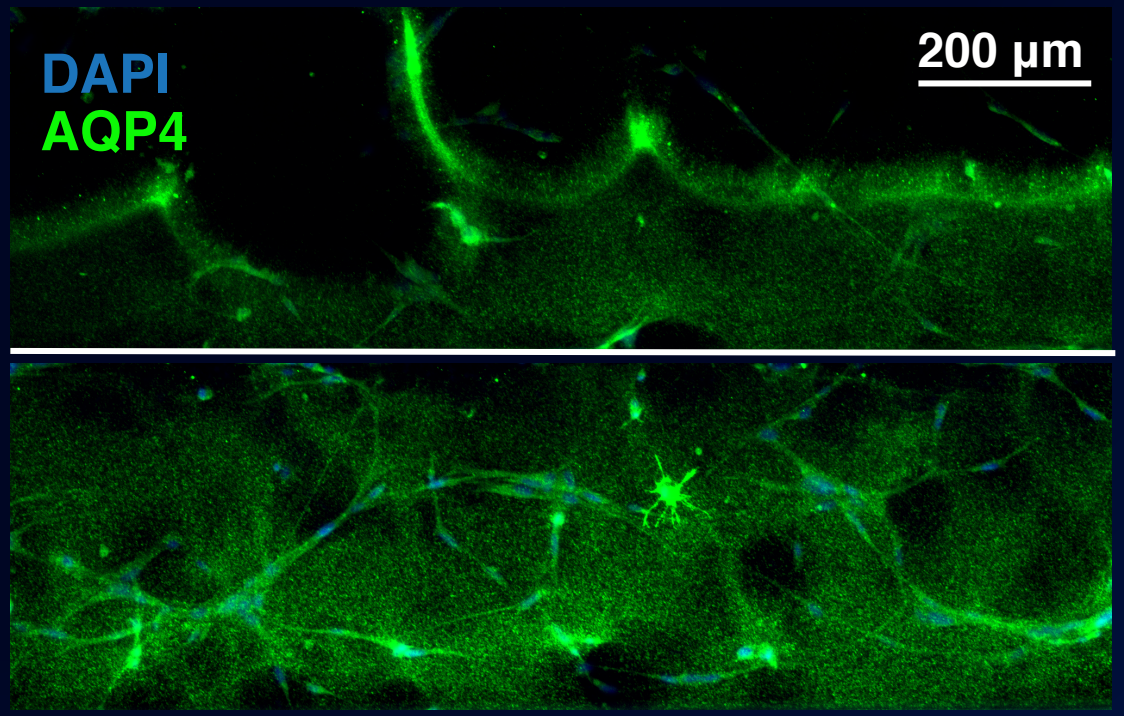

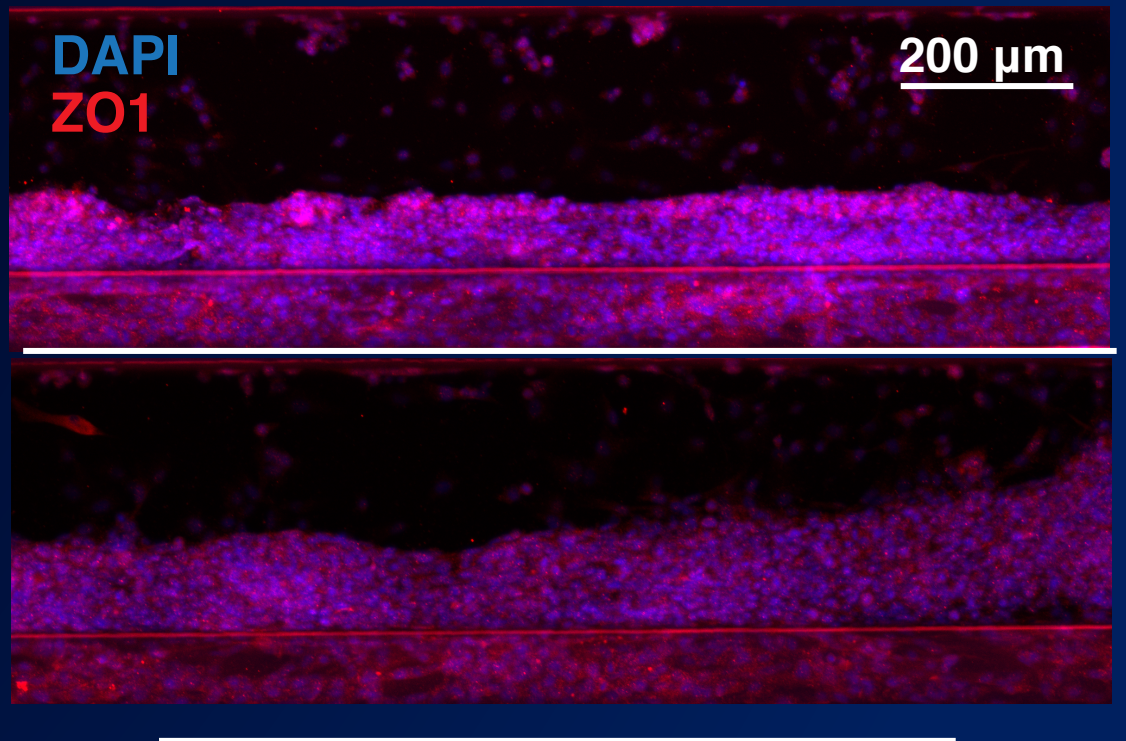

Acute Responses to Radiation:
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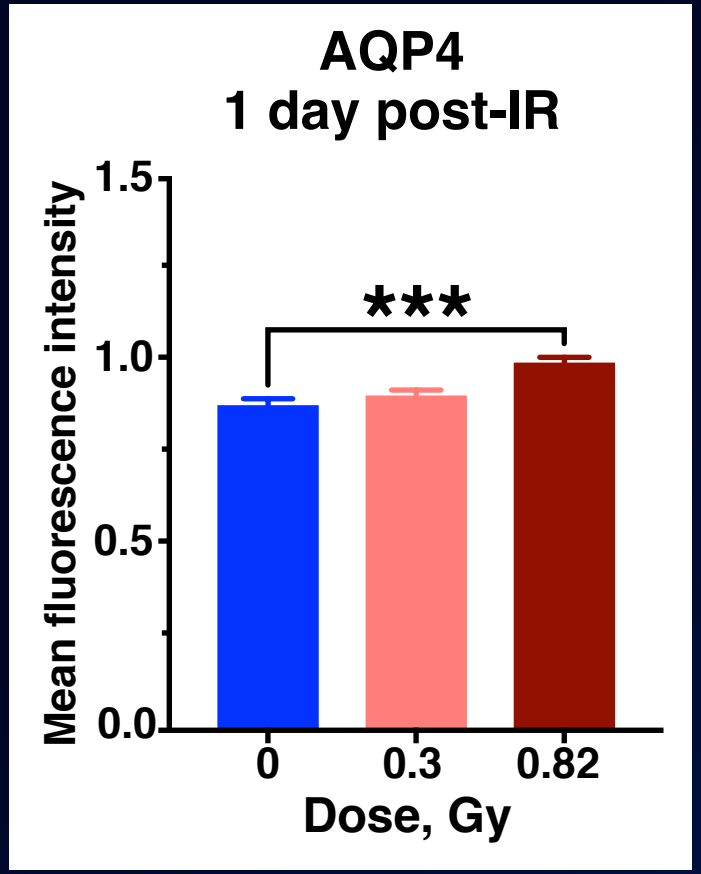
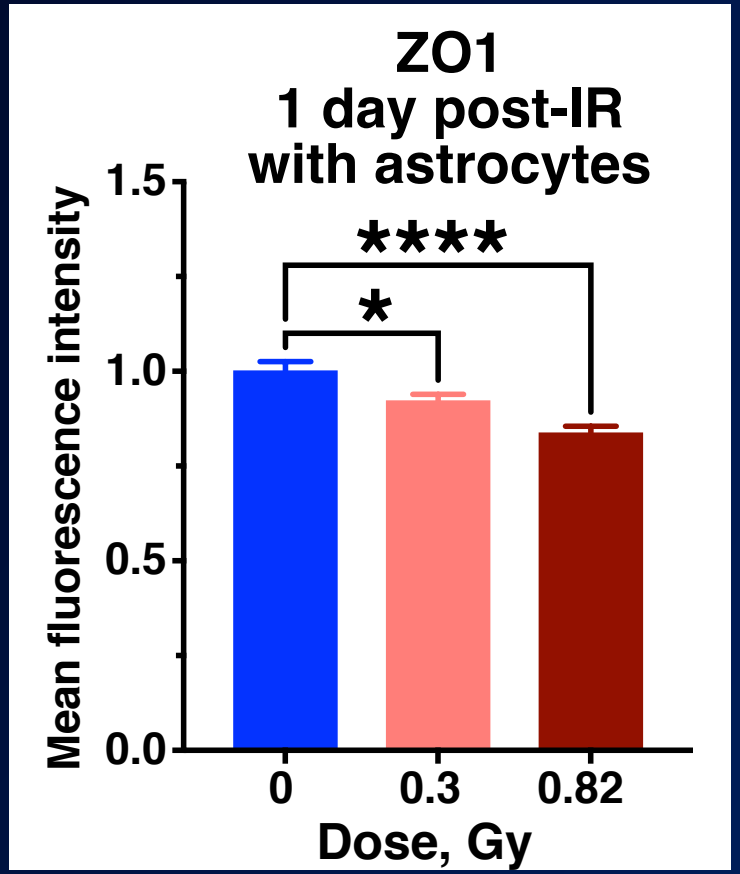
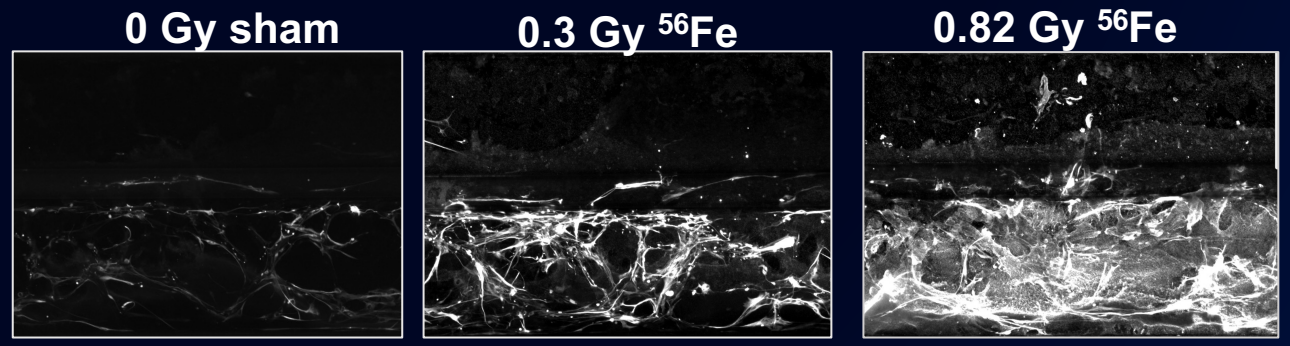
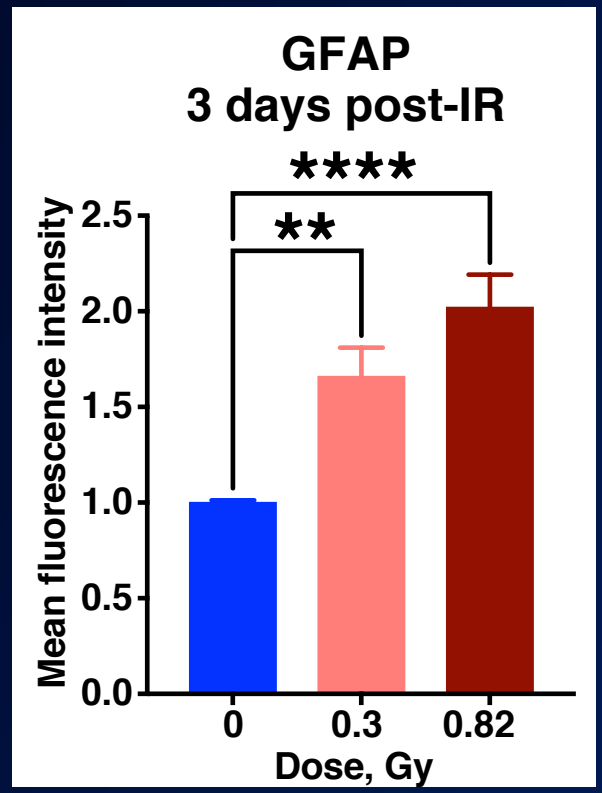


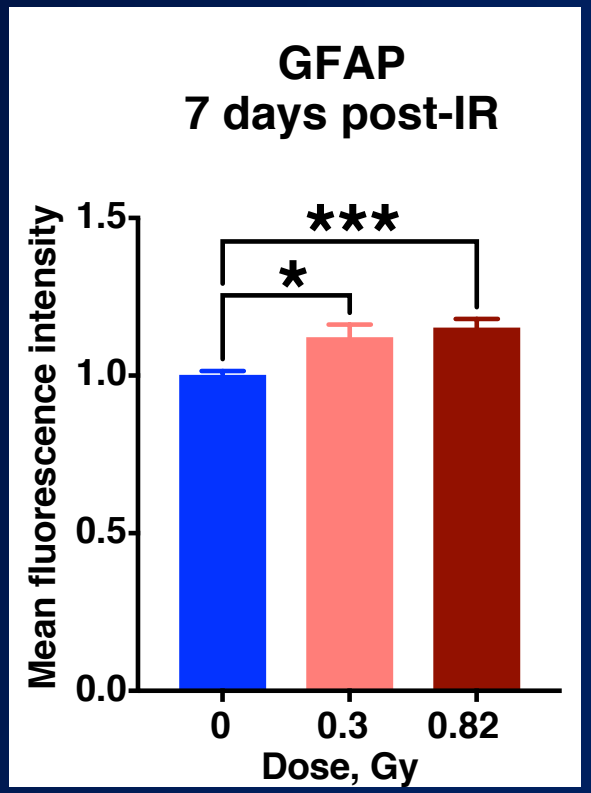


Subacute Responses to Radiation:
Astrocytes Adopt Scar-Like Phenotype

600MeV/n ^{56}Fe particles







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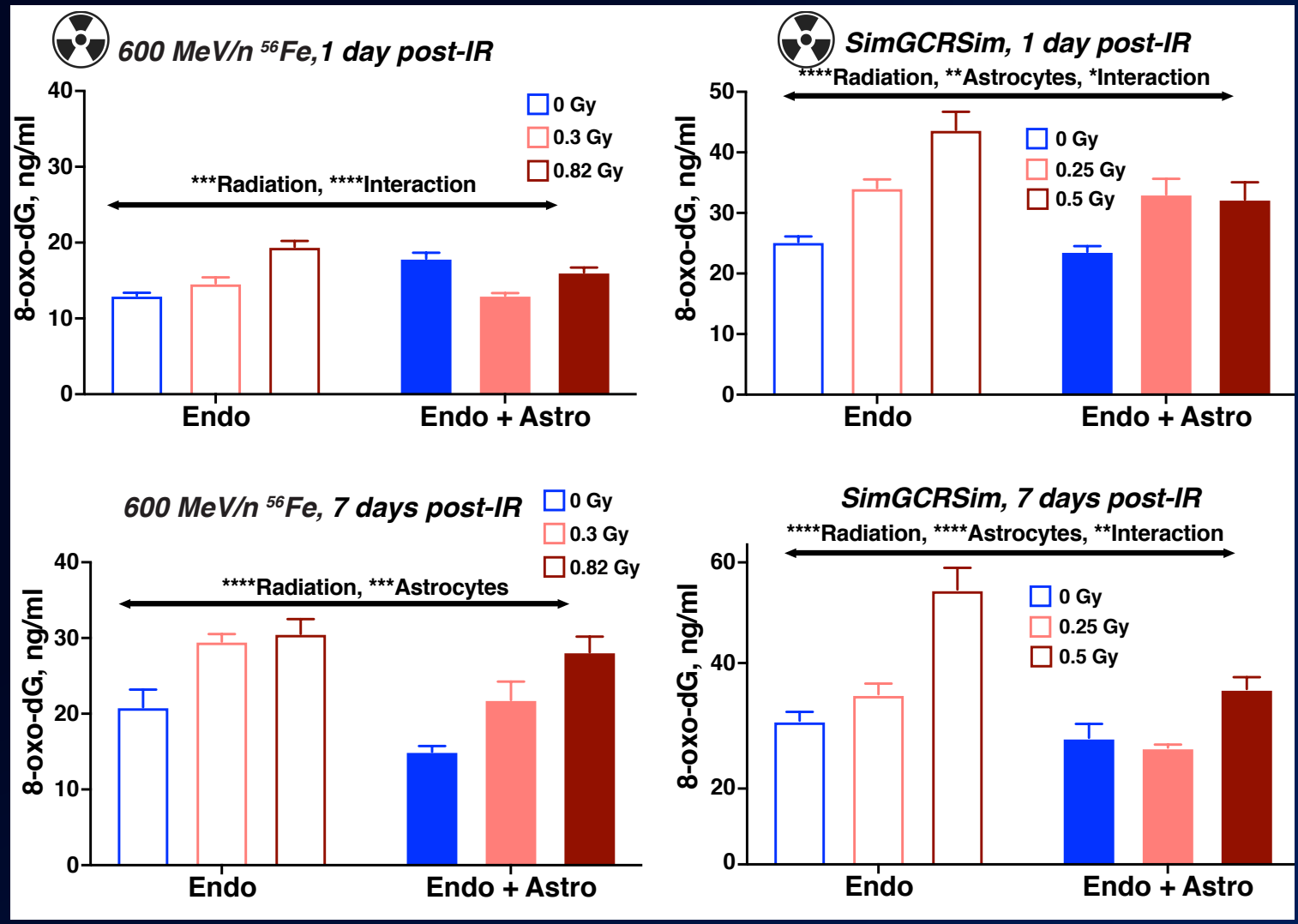
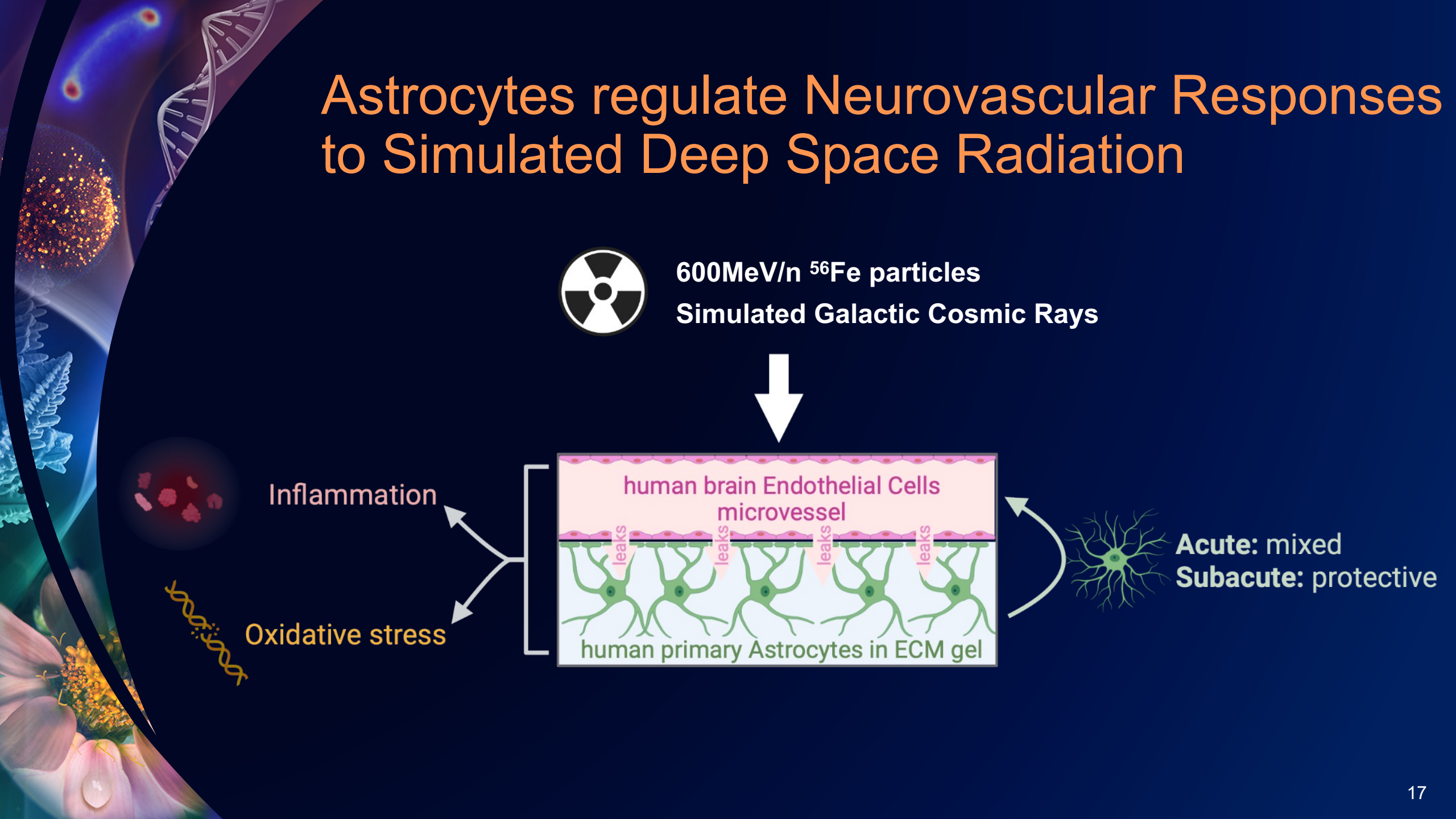
Astrocytes Limit Oxidative Stress Induced by Radiation



Astrocytes regulate Neurovascular Responses to Simulated Deep Space Radiation



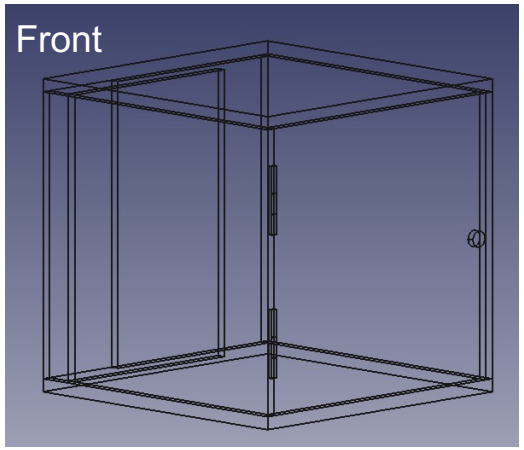
Dose-Rate Effects of Ionizing Radiation on a Neurovascular model

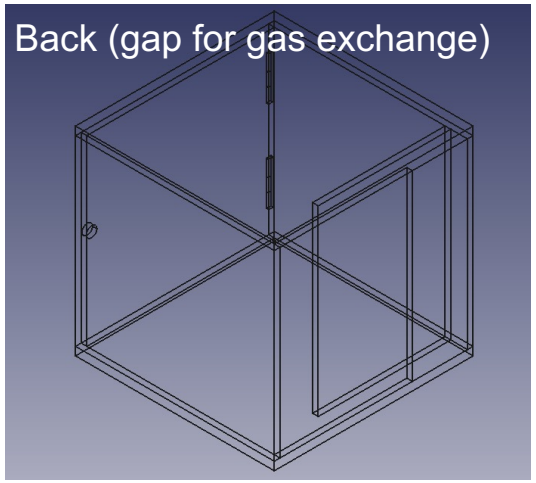
Chronic gamma radiation (^{57}Co plate)

Dose-Rate Effects of Ionizing Radiation

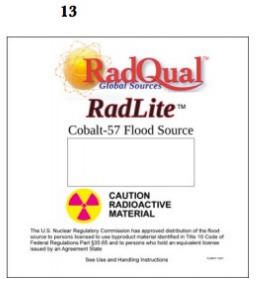
Environmental chamber

Leaded acrylic enclosure





Chronic gamma radiation ^{57}Co plates



Flood Sources

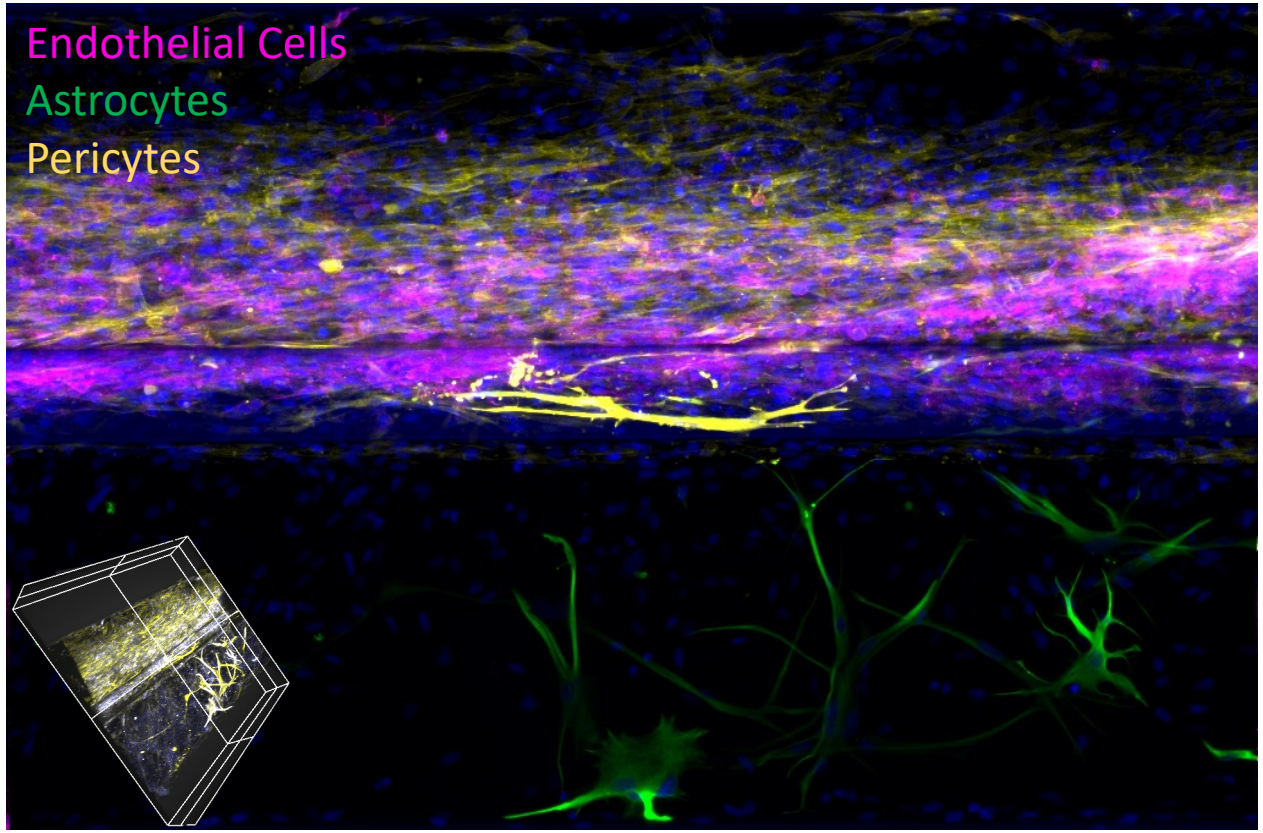
Retangular Series
BM01, BM04 & BM07

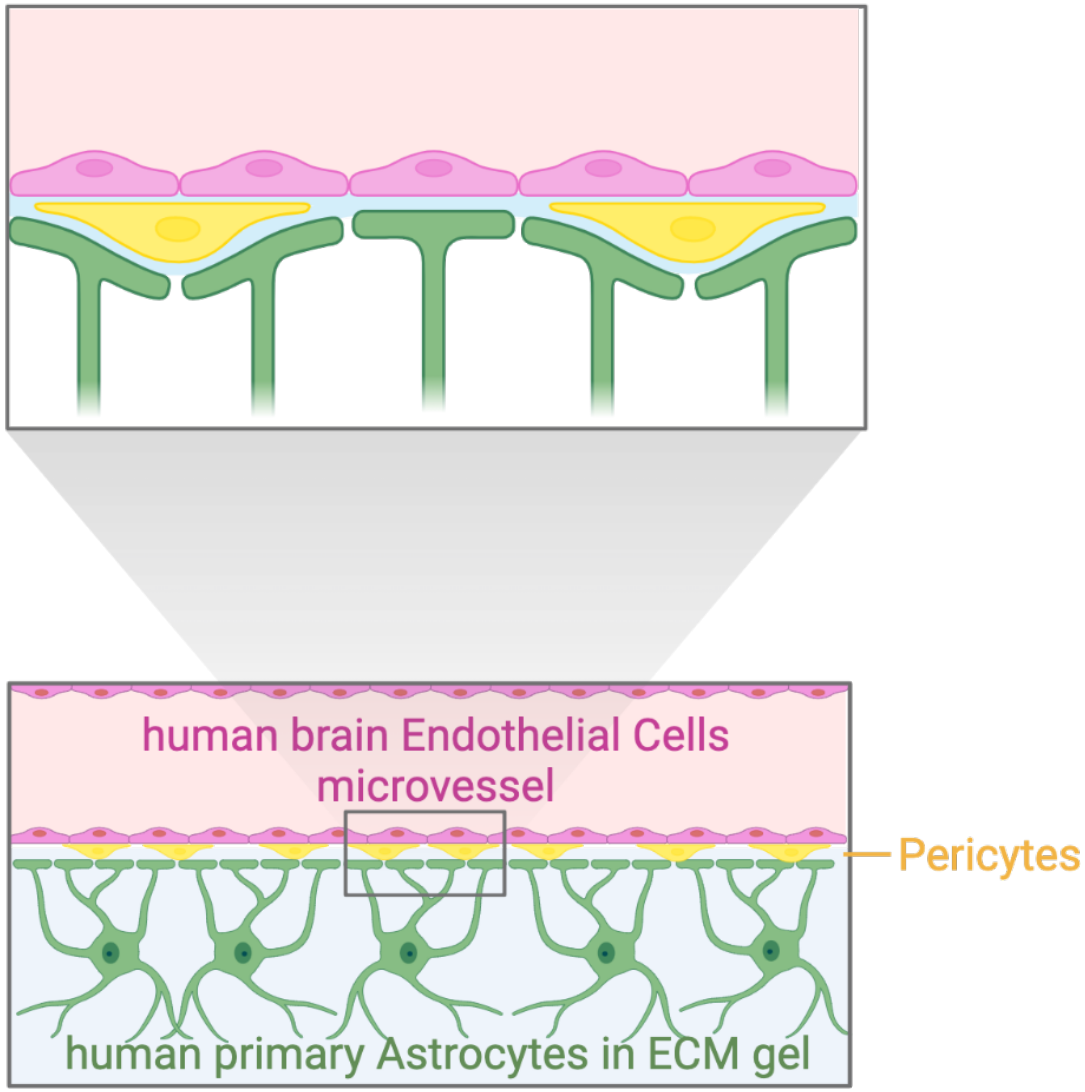
Series	Weight	Overall Dimensions (Inches)	Thickness	Co-57 Matrix	Activity
BM01L	7lbs.	24.1" X 16.7"	0.35"	23.9" X 16.5"	5, 10, 15 or 20 mCi
BM02	5lbs.	20.3' round	0.7"	18.5" round	5, 10 or 15 mCi
BM04	5lbs.	19.6" X 15.6"	0.7"	18" X 14"	10, 15 20 mCi
BM05	2lbs.	11.5" X 11.5"	0.7"	10" X 10"	0.5, 3, 10, 15 or 20 mCi
BM07	3lbs.	15.8" X 9.5"	0.3"	15.5" X 9.3"	7.5, 10 or 15 mCi

Square Series
BM05 & BM05-99*
*Exclusive for Dilon 6800 0.5 mCi to 3.0 mCi activity

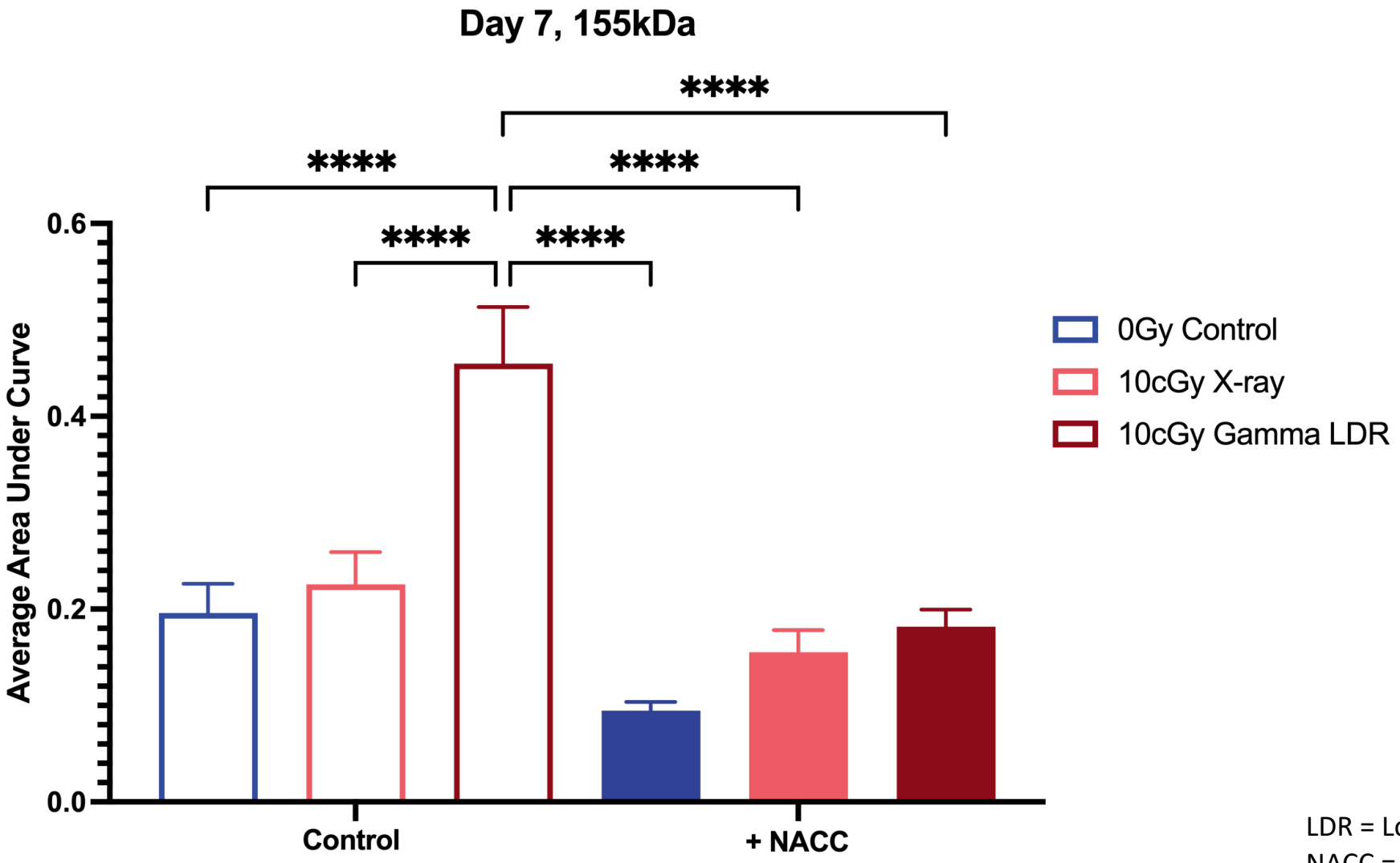
Circular Series BM02

Improved Neurovascular Model



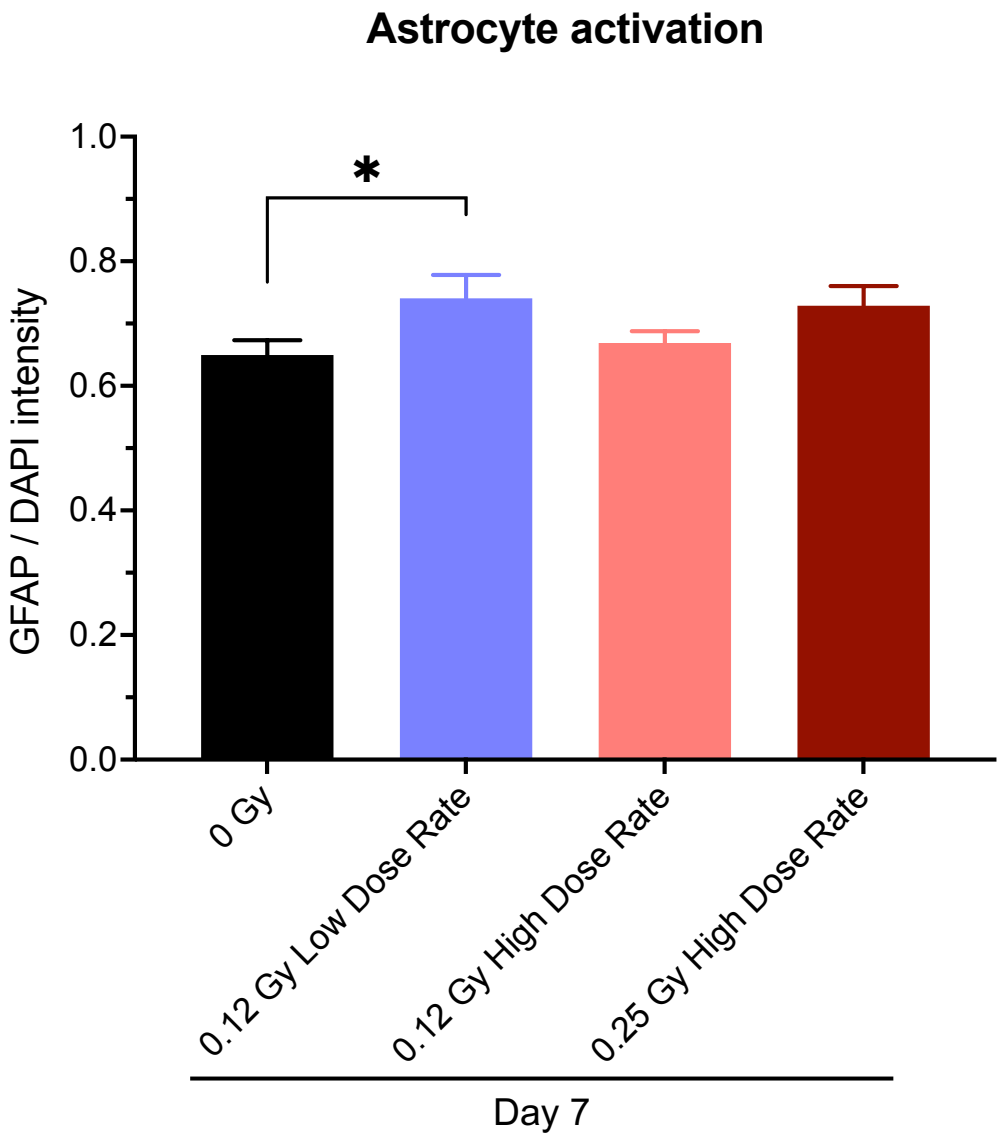


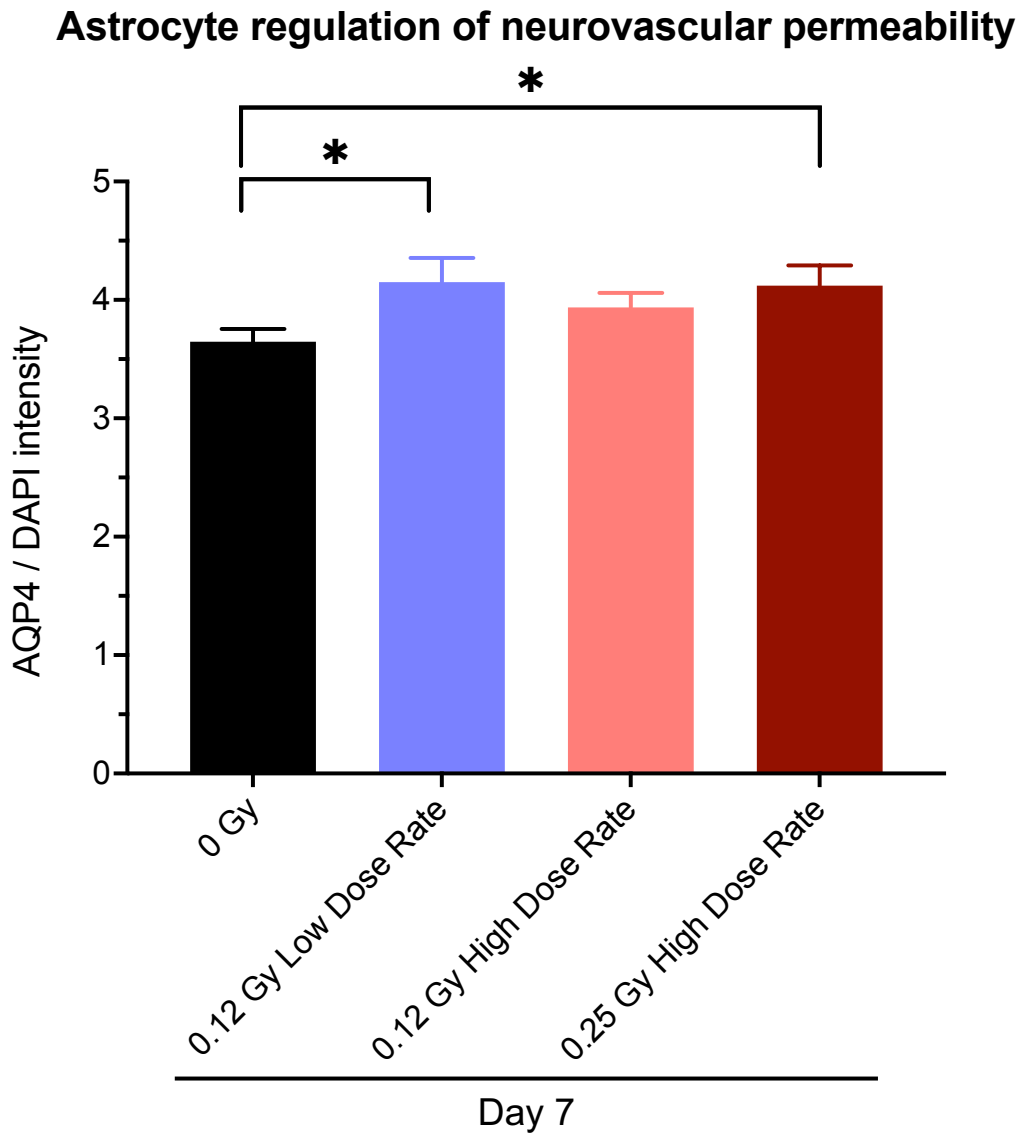
Dose-Rate Effects of Ionizing Radiation: Chronic vs. Acute



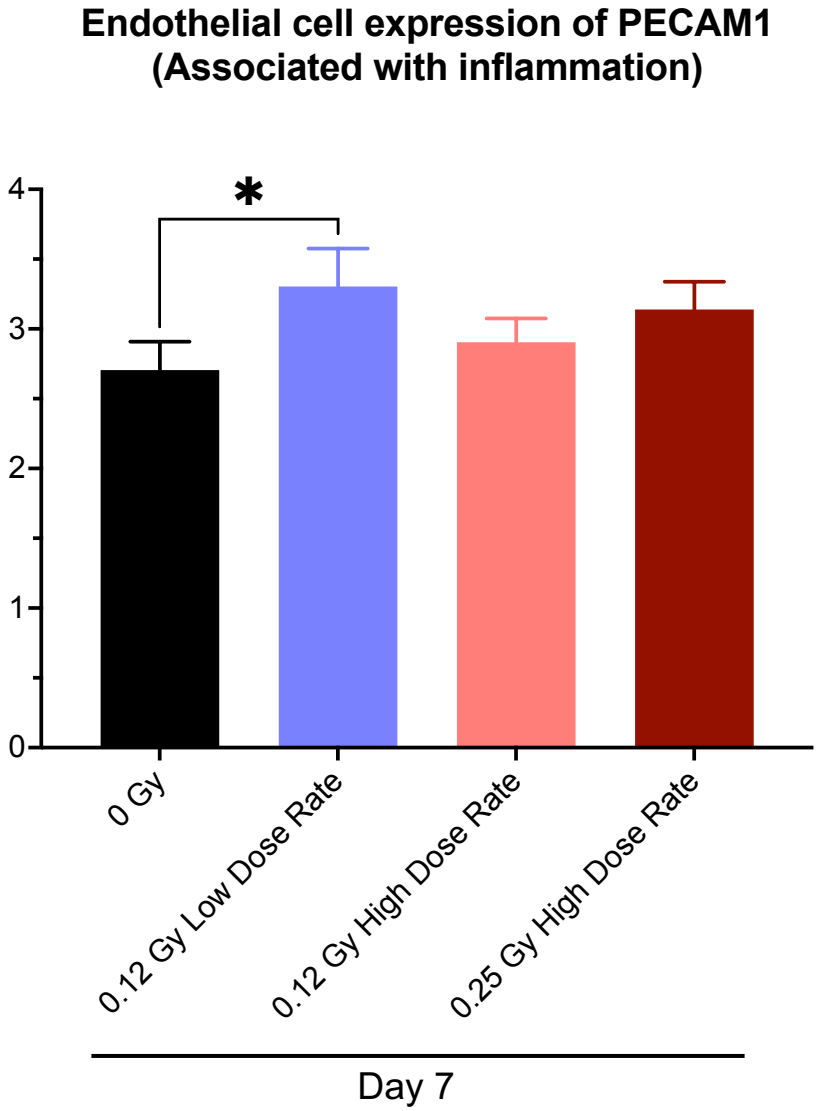
LDR = Low Dose-Rate
NACC = N-acetylcysteine

Dose-Rate Effects of Ionizing Radiation: Chronic vs. Acute





Dose-Rate Effects of Ionizing Radiation: Chronic vs. Acute



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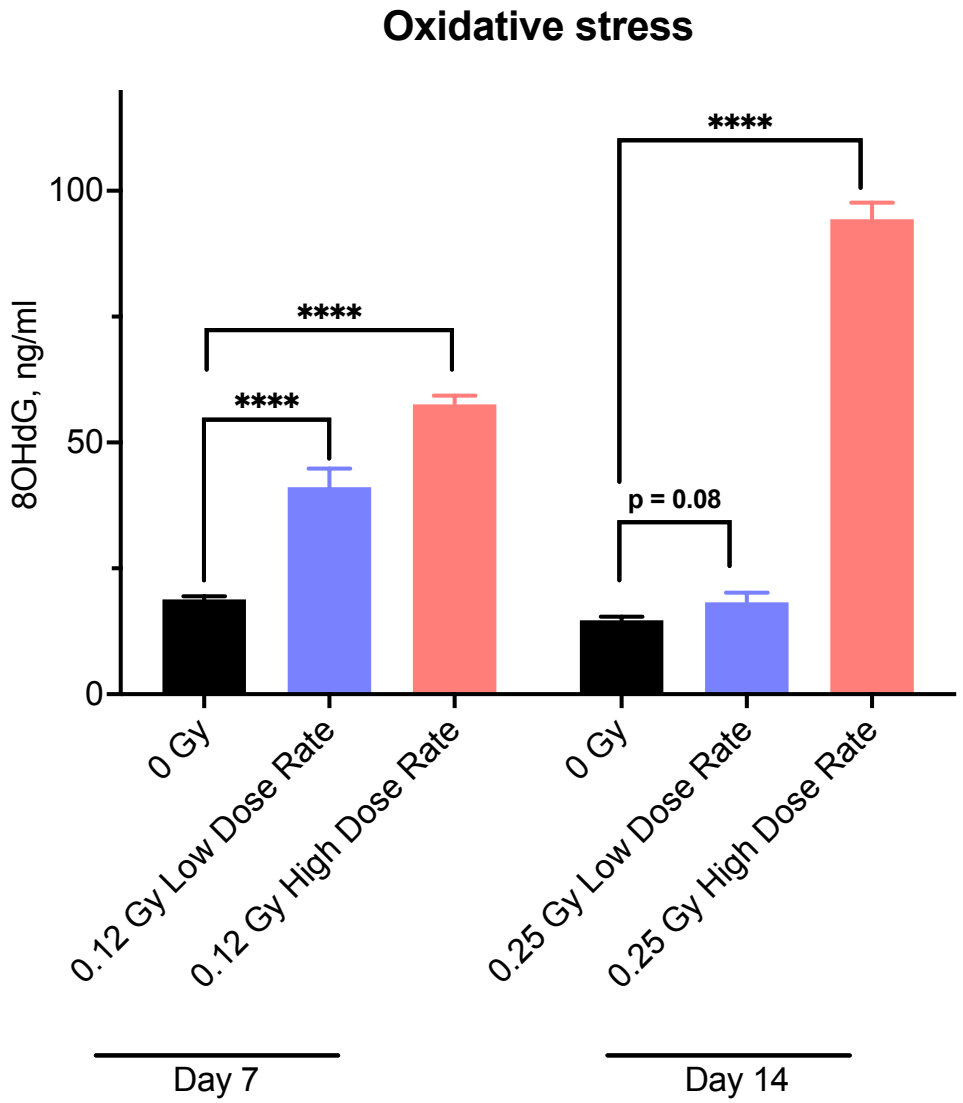

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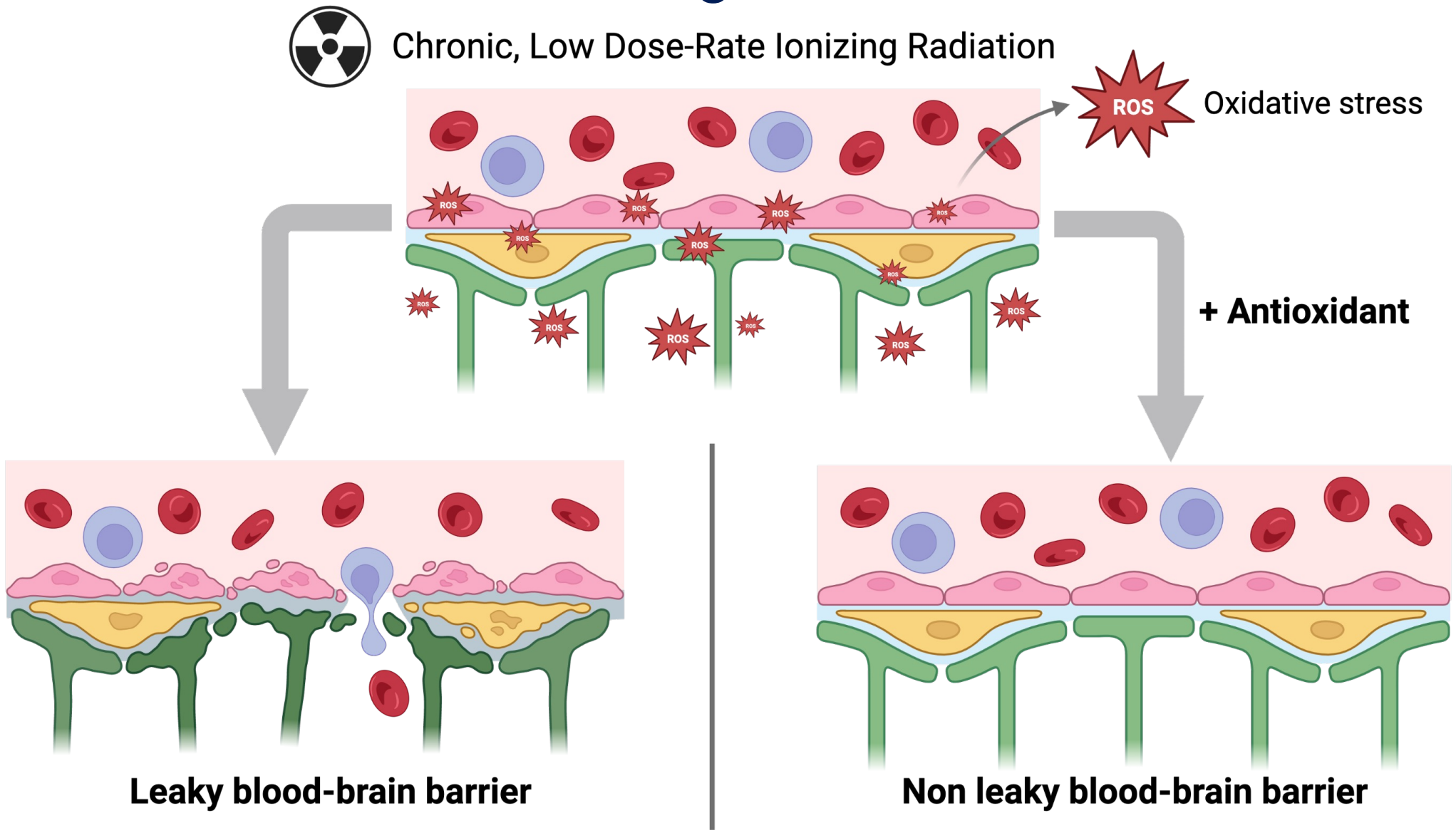
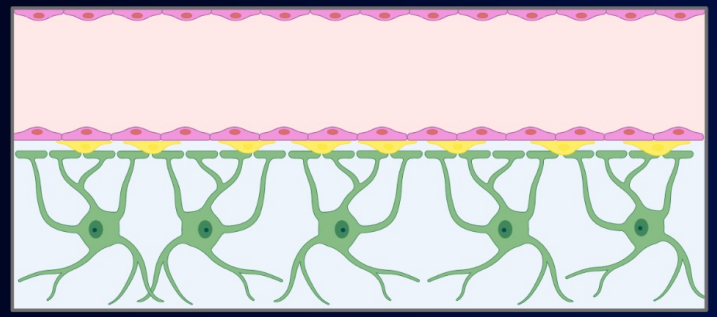


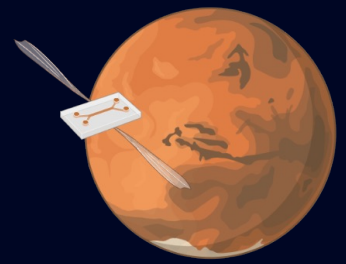
Future Directions

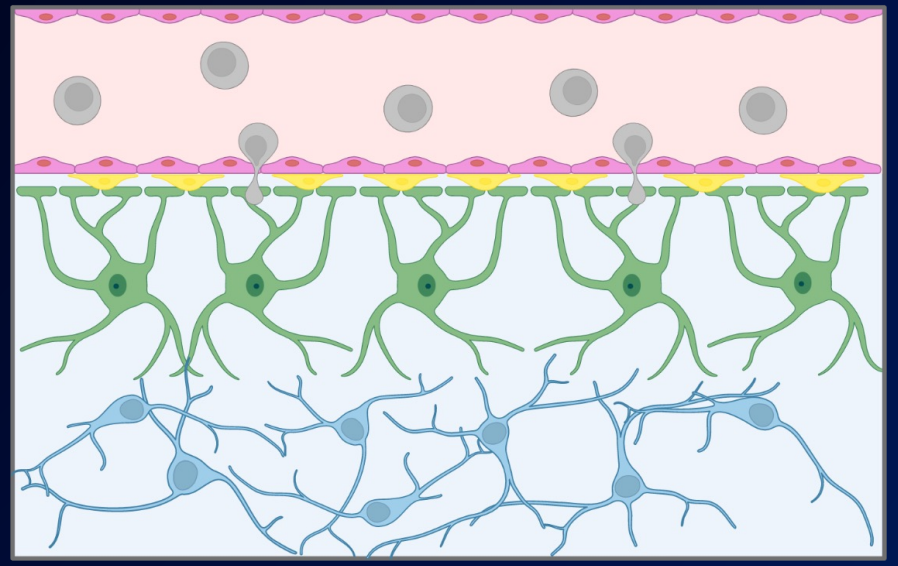
Long-lasting organ models



Neurovascular model

Payload adaptation





+ Immune cells

+ Neurons

Acknowledgments

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Nienke Wevers

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NASA Ames ARIA

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